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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/836,911	04/17/2001	Gyula Hadlaczky	24601-402I	7763
20985	7590	01/11/2005	EXAMINER	
FISH & RICHARDSON, PC 12390 EL CAMINO REAL SAN DIEGO, CA 92130-2081			SHUKLA, RAM R	
			ART UNIT	PAPER NUMBER
			1632	

DATE MAILED: 01/11/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.

09/836,911

Applicant(s)

HADLACZKY ET AL.

Examiner

Ram R. Shukla

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-- Th MAILING DATE of this communication app ars on th cover sheet with the correspond nce address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 25 October 2004.
- 2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 23-60 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 23-60 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
- ☐ Certified copies of the priority documents have been received.
 - ☐ Certified copies of the priority documents have been received in Application No. _____.
 - ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- * See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|--|---|
| 1) <input type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413)
Paper No(s)/Mail Date. _____ |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152) |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)
Paper No(s)/Mail Date _____ | 6) <input type="checkbox"/> Other: _____ |

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DETAILED ACTION

1. A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 10/25/04 has been entered.

2. Claims 23-60 are pending in the instant application.

Claim Rejections - 35 USC § 112

3. The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

4. Claims 23-60 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention, for reasons of record set forth in the previous office action of 12-18-2002 and 3/23/04. Applicants have amended claims 23, 24, 26, 51, 52, 54, 55 and 56 by limiting nuclear donor cell to a mammalian cell, transferring nucleus into an enucleated cell of the same species and that the recipient cell is transferred into a non-human mammal that is of the same species as the nucleus recipient cell. However, these amendments do not address the enablement rejection raised in the previous office actions and therefore the rejections are maintained for reasons of record.

Response to Arguments

Applicant's arguments filed 10/25/04 have been fully considered but they are not persuasive.

Applicants on page 3, paragraph labeled I argue that the rejection confuses enablement and utility rejection. In response it is clarified that the rejection set forth in the previous office action and reiterated in the instant office action is only an enablement rejection and not a utility

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rejection and nowhere in the office action a utility rejection was set forth is set forth. Therefore, there is no confusion regarding enablement rejection and utility rejection and the enablement rejection is analyzed based on how to make and how to use as required by 112 first paragraph.

Next, in paragraph labeled II, applicants reiterate their argument that all pending claims are not in the purview of the rejection for not enabling generation of a transgenic animal. However, it is reiterated that the only intended use for the claimed method is for making a transgenic animal. Applicants argue:

The Examiner asserts in the Advisory Action that the rejection is proper because the "intended" use of Claims 23, 24, 25, 27-30, 32-39 and 41-56 is for generation of a transgenic animal. As Applicant respectfully submits, however, in the section below rebutting the Examiner's assertions in the Advisory Action (*see* page 19), the Examiner provides no substantiation for the bald assertion that the only intended use of the claims is for generation of a transgenic animal. Moreover, the relevant question with regard to enablement

It is noted that examiners' statement in the advisory action was not a bald assertion; rather it was made after reviewing specification. It is for applicants to provide evidence as to where in the specification there was support for any other use for the claimed method. It is emphasized that while applicants have submitted a twenty-nine page response to the office action, they did not indicate as to where in the specification another intended use for the claimed method was disclosed.

Regarding the enablement rejection applicants have reiterated the same arguments as in the previous response. In discussing *In re Scarbrough*, applicants have argued that the instant specification teaches exactly how to perform each step and list page 11, lines 14-18 as an example. However, these arguments are not persuasive because the specification does not provide any specific guidance to practice the claimed method, except for a general disclosure. Applicants have not indicated as to where in the specification the method for first removing a nucleus from a donor cell and then transferring the nucleus in a donor cell and transferring the resultant cell into an animal to produce a transgenic animal. It is emphasized that as has been discussed in the previous office actions these steps are unpredictable and were not routine in the art and in the absence of any specific guidance from the specification an artisan could not practice the claimed method without undue experimentation.

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Applicants' arguments on page 6 about the Wilmut article are reiteration of what was discussed in the previous response. Additionally, applicants' discussion of what is taught in the specification is not relevant to the instantly claimed method because none of the discussed techniques (see the second full paragraph on page 6) are directed to the claimed methods. On page 7, applicants argue:

The Examiner appears to be alleging that the information "lacking" in the record is a teaching in the specification of how to adapt the disclosed method to different cell types from different species. The Examiner points to the alleged "unpredictability" of nuclear transfer as the basis for this allegation, and in previous Office Actions has cited several post-filing references in support of this assertion. As discussed below, however, the specification, in light of the

However, these arguments are not persuasive since the method of nuclear transfer at the time of the invention was not predictable and routine and the specification did not provide any specific guidance for practicing the claimed method.

Applicants then argue that examiner has used several post filing arts in support of unpredictability allegation. It is noted that examiner did not use only post filing art. It fact art discussed were from the time of the invention to later on to demonstrate that even post filing the method of making a transgenic animals by nuclear transfer was not a routine method. Applicants citing references as discussed in the second full paragraph on page 9 did not make the method routine because none of these references teaches the claimed invention of making a transgenic animal by nuclear transfer wherein a gene of interest is introduced in the nucleus of a donor cell using artificial chromosome. Examiner has demonstrated that the art of first introducing an exogenous DNA via an artificial chromosome into a cell and then transferring the nucleus of the cell to a recipient cell which is then transferred in an animal to make a transgenic animal was not routine at the time of the filing and even post filing and the specification does not provide any specific guidance except for general description. As noted in the office action of 12/18/02 (see page 3, last paragraph continued on page 4) and reiterated below, the specification has a 17-line disclosure about nuclear transfer.

First, the only teaching in the specification about nuclear transfer method for producing a transgenic animal is on page 52, lines 22-32 continued in lines 1-7 on page 53 and the description recites Wilmut et al 1997, a nature article and two world documents which are applicants' there own and which have been issued as US patents 6,025,155 and 6,077,697. It is emphasized that these two patents by

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It is emphasized that combined with the state of the art and the 17 line disclosure in the specification an artisan of skill would not have been able to practice the claimed invention without undue experimentation as discussed in the previous office actions and in the instant office action.

Next, applicants in their argument in section (2) on page 12 discuss lack of utility. These arguments are irrelevant because there is no lack of utility rejection and therefore these arguments will not be addressed. Applicants argue:

"In the reasons of record in previous Office Actions, the Examiner alleges that the method of Wilmut et al., described in the disclosure and incorporated by reference therein, does not provide an enabling disclosure because this method allegedly has not been reproducible in other laboratories (citing Wolf et al., J. Biotechnol. , 65:99- 110 (1998)). Applicant respectfully submits that in making this statement, the Examiner is asserting a lack of utility of the method of nuclear transfer as taught in the specification because the method allegedly is "inoperative." The remaining post-filing date references cited by the Examiner and discussed above under "lack of enablement" also go to an allegation of lack of operability and may properly be applied in a rejection on grounds of lack of utility under 35 U.S.C. 101."

The Examiner disagrees with this assertion of the applicants because Wilmut art was the first art to report nuclear transfer and arts following that e.g., Wolf et al showed that the method could not be reproduced as taught by Wilmut. In light of arts that showed successful nuclear transfer in selected examples, the state of the art of nuclear transfer and making a transgenic animal comprising nuclear transfer was not routine and was unpredictable and therefore claimed method required specific guidance. Therefore, It is reiterated, though, that the issue regarding the method of Wilmut being not reproducible was unpredictability in light of the other publication and therefore is relevant to lack of enablement and not utility. Applicants have argued utility issue in pages 12-19, however these arguments have not been addressed because the office action did not set forth a utility rejection.

Under the heading "Rebuttal to specific issuein the Advisor action " on pages 19-28, Applicants have not provided any new evidence of substance, rather reiterated the same or similar arguments as addressed above and therefore these arguments have not been separately addressed again.

Finally on page 28, last paragraph, under the heading "Policy" applicants argue:

"As taught in the above-captioned application, any methods known in the art pertaining to introduction of foreign genes carried in traditional, standard sources (such as genes harbored in expression vectors) into cells for any variety of purposes, e.g., gene therapy, protein production and the generation of transgenic animals, including

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nuclear transfer methods, can be applied in similar fashion to the introduction of artificial chromosomes, particularly SATACS, into cells. The application describes and demonstrates that once the artificial chromosomes are generated and isolated and/or introduced into cells, then any known procedure that has previously been performed with any heterologous gene from any source is applicable to the SATACS (as well as the minichromosomes) carrying foreign genes of interest."

In response it is noted that applicants seem to have ignored the fact that all these methods and inventions listed in their arguments- gene therapy, protein production and the generation of transgenic animals, including nuclear transfer methods- are all not trivial and routine methods and they require specific guidance to practice which the instant specification lacks.

In conclusion, the specification as filed is not enabling for the claimed invention because the state of the art of producing transgenic animals from any donor cell into any recipient cell and for transfer of artificial chromosomes in a cell that could serve as donor cell was not predictable and an artisan of skill would have required extensive experimentation to practice the claimed invention and such experimentation would have been undue since the experimentation was not routine, and the state of the art was unpredictable and the specification did not teach how to address the limitations and unpredictable nature of the invention.

5. No claim is allowed.

All claims are drawn to the same invention claimed in the application prior to the entry of the submission under 37 CFR 1.114 and could have been finally rejected on the grounds and art of record in the next Office action if they had been entered in the application prior to entry under 37 CFR 1.114. Accordingly, **THIS ACTION IS MADE FINAL** even though it is a first action after the filing of a request for continued examination and the submission under 37 CFR 1.114. See MPEP § 706.07(b). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire **THREE MONTHS** from the mailing date of this action. In the event a first reply is filed within **TWO MONTHS** of the mailing date of this final action and the advisory action is not mailed until after the end of the **THREE-MONTH** shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however,

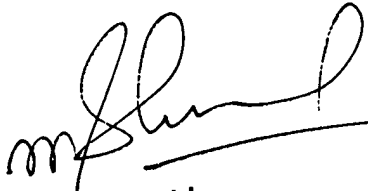
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will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Ram R. Shukla whose telephone number is (571) 272-0735. The examiner can normally be reached on Monday through Friday from 7:30 am to 4:00 p.m. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Amy Nelson, can be reached at (571) 272-0804. The fax phone number for TC 1600 is (571) 273-8300. Any inquiry of a general nature, formal matters or relating to the status of this application or proceeding should be directed to the Dianiece Jacobs whose telephone number is (571) 272-0532.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Ram R. Shukla, Ph.D.
Primary Examiner
Art Unit 1632


**RAM R. SHUKLA, PH.D.
PRIMARY EXAMINER**